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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,415	07/29/2003	Ludger Johannes	2121-0176P	6282
2292	7590	08/02/2005	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO.BOX 747 FALLS CHURCH, VA 22040-0747			MINNIFIELD, NITA M	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 08/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/628,415	Applicant(s) JOHANNES ET AL.	
	Examiner N. M. Minnifield	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 9-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 9-24 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed April 27, 2005 is acknowledged and has been entered. The claims have not been amended. Claims 1-8 are now pending in the present application. All rejections have been withdrawn in view of Applicants' comments, with the exception of those discussed below.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Claims 9-24 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention(s), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 4, 2004.
4. The disclosure is objected to because of the following informalities: there are letters missing from words through out the specification, see for example p. 6, l. 28, p. 15, l. 31 and p.16, l. 31. Applicants should review the entire specification and make corrections where necessary. Appropriate correction is required.

Applicants have stated that they have carefully reviewed the identified specification pointed to by the Examiner and fail to find any misspelled terms or letter missing. Examiner is referring specifically to, for example, page 16, line 31, "Carlsson t al", should be "Carlsson et al". It appears that the missing letters

may have something to do with the scanning process, as other specifications have letters missing from words. Perhaps, Applicants could review the specification found on the Public PAIR system to ensure that the specification is correct.

5. The objection to the specification and rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph is withdrawn in view of the deposit information provided on plasmid pSU108 having SEQ ID No. 2 integrated between the SphI and Sall restriction sites, and the corresponding cell line has been deposited at CNCM on December 19, 2000 with the registration number 1-2604. The certificate of deposit has been provided and the appropriate statements of assurance been made.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
9. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haicheur et al 2000 (J. Immunology, 2000, 165:3301-3308) in view of Wang et al (WO 95/11998).

Haicheur et al teaches a construct of the B subunit of Shiga toxin fused to a tumor peptide (abstract). The prior art teaches that the Shiga B subunit acts as a vector (i.e. carrier) (see abstract; p. 3301, col. 2). Haicheur et al teaches that the "Shiga B subunit targets this pathway in a receptor-dependent manner, namely via binding to the glycolipid Gb3. Because this receptor is highly expressed on various dendritic cells, it should allow preferential targeting of the Shiga B subunit to these professional APCs. Therefore, the Shiga B subunit appears to represent an attractive vector for vaccine development due to its ability to target dendritic cells

and to induce specific CTL without the need for adjuvant.” (abstract) Haicheur et al teaches that different peptides and proteins (i.e. OVA, SL8, P815A and P1A) can be fused to the Shiga B subunit (materials and methods, p. 3302, col. 1). Haicheur et al teaches the STxB subunit and Z(n) wherein the Z can be a polypeptide (i.e. tumor peptide). The prior art does not teach the cysteine residues. However, it is well known in the art to add cysteine residues to synthetic peptides for polymerization. Wang et al teaches that extra residues can be added to the ends of the SSAL (structured synthetic antigen libraries) and that KKK can be added at the amino terminus to increase peptide solubility, cysteine can be added to facilitate directed coupling to carrier molecules, and methionine can be added for cyanogen bromide cleavage if necessary. Wang et al teaches that the SSAL can be a domain within a peptide or can have other antigenic, diagnostic or therapeutic sites attached to it. The SSAL can be attached to a core sequence for facile delivery. These core sequences include branched cores, which can be an amino acid or an amino acid analog having two amino groups and one carboxyl group, each group capable of forming a peptide bond linkage. Preferably such amino acids are lysine or a lysine analog such as ornithine (see p. 20; p. 23). Wang et al teaches that “...SSAL can also be used to form conjugates, i.e., the SSAL, either in branched or linear form can be coupled directly or indirectly, by methods known in the art, to carrier proteins such as bovine serum albumin (BSA), human serum albumin (HSA), or to red blood cells or latex particles.” (p. 21, lines 13-19) Since the prior art teaches that carriers (i.e. STxB, BSA, HSA etc) can be coupled directly or indirectly to a polypeptide and that the cysteine is added to facilitate coupling it would have been obvious to a person of ordinary skill in the art to combine to teachings of Haicheur et al in view of Wang et al to prepare a

composition comprising the formula a STxB-polypeptide-cysteine (STxB-Z(n)-cys) for the purposes of targeting molecules to Gb3. The specification teaches that B-subunit of *Shigella dysenteriae* is an homopentamer protein (5B--fragments) and is responsible for toxin binding to and internalization into target cells by interacting with the glycolipid Gb3 found on the plasma membranes of these cells (p. 1, l. 11-14), which is what the prior art teaches. The claimed invention is prima facie obvious in view of the combined teachings of Haicheur et al in view of Wang et al, absent any convincing evidence to the contrary.

Applicants have asserted that the Examiner has failed to properly support a rejection for prima facie obviousness and that there is not suggestion or motivation provided to modify Haicheur et al or to combine the reference teachings with Wang et al to establish prima facie obviousness. Applicants have asserted that Wang et al fails to contain any working examples or provide any results/data regarding the use cysteine residue to facilitate directed binding of a peptide to a carrier and no carrier molecule is disclosed or discussed in Wang et al. More importantly, Wang et al fails to disclose or suggest the binding of a peptide, through a cysteine residue, to a carrier that will target the peptide to a specific pathway via receptor binding, such as is accomplished with the present invention and the Shiga B subunit. There is no suggestion or prediction in Wang et al as to whether construct containing the cysteine residue would still target to the desired pathway. Applicants have asserted that Wang et al. discloses that the cysteine residues may be added either the N-terminus the C-terminus peptide to facilitate binding to the carrier. However, Wang et al fails to teach the site of the carrier where the cysteine residue bound to the peptide can be coupled so that the carrier

function will not be impaired.

However, it is noted that the pending claims do not recite any limitations with regard to “specific pathway” or “target to the desired pathway”. Further, Wang et al, teaches that the cysteine can be added to facilitate directed coupling to carrier molecules. Because this concept is taught in the art, there is a reasonable expectation of success of making the claimed composition having the claimed formula, since Wang et al teaches that coupling the cysteine can be added to facilitate coupling to the carrier. Applicants and Haicheur et al use the STxB subunit for the same purpose of targeting molecules to Gb3. With regard to Applicants assertions regarding the whether the cysteine is added to the N-terminus or C-terminus of the peptide, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to optimize the formula for the composition by using the terminus that provided a better universal polypeptidic carrier. It would have been obvious to one having ordinary skill in the art at the time the invention was made to couple the cysteine to the terminus (N- or C-) that does not alter the function of the carrier, since it has been held that discovering an optimum components of a composition are only routine skill in the art. *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980). The claimed invention is prima facie obvious in view of the combined teachings of Haicheur et al in view of Wang et al, absent any convincing evidence to the contrary.

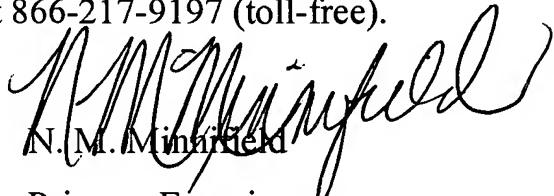
10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is

571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM

July 20, 2005